# Sequelae of Bacterial Meningitis in Infants

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■ *Electroencephalograms, developmental tests and intelligence tests indicated that six of ten children under two years of age who had purulent meningitis, had apparent permanent neurological damage. The data suggested that this damage may be related in part to the occurrence of subdural effusions.*

*Serial electroencephalograms and developmental tests appeared useful for suggesting which patients might retain a high risk of compromised brain function.*

*The lack of further decrease in mortality from this disease in recent years may be because of cases in which meningitis is "secondary" to a primary disease of the central nervous system—that is, due to operation for brain tumor or myelomeningocele which affords direct entry of organisms. The incidence of permanent sequelae following this disease may not be decreasing.*

ALTHOUGH DIAGNOSIS and therapy of bacterial meningitis are reasonably clear, little is known of the wastage of this disease—that is, the number who die or suffer from permanent sequelae. For light on this aspect, follow-up observation of a group of patients was maintained for two years.

## Method of Procedure

Ten patients under two years of age who were treated for purulent meningitis between September 1959 and June 1960 were studied prospectively. Detailed information concerning the onset of the illness and developmental characteristics was obtained from the family and referring physician upon admission. An electroencephalogram was obtained during or at the end of the acute illness, another six months later, and a third two years later. A developmental test as devised by Gesell[8] was performed one month after the acute illness, one year following the acute illness, and, if indicated, at intervals before or after this. The Stanford-Binet Intelligence Test was performed two years following the acute illness and the parents were interviewed about developmental and behavioral characteristics. On the basis of the data obtained the patients were then rated as to present neurological state in the following manner: 0 indicated all data to be normal; 1+ indicated one or more "minor" manifestations (behavior problems,

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TABLE 1.—*Data on Ten Cases of Purulent Meningitis in Patients Under Two Years of Age (1959-1960)*

| Patient | Status 2½ Years After Illness | Brain Damage Rating | Age at Onset | Organism Cultured | Subdural Effusion | EEG | | | After Illness | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | During Treatment | After Illness | | | | |
| | | | | | | | Months | Interpretation | Months | Developmental Quotient | I.Q. |
| 1. | Normal | 0 | 2 weeks | Hemophilus influenzae | Yes, no operation | Very abnormal | 1 | Normal | 1 | 100 | 100 |
| | | | | | | | 30 | Normal | 12 | 110 | ..... |
| 2. | Normal | 0 | 12 months | Hemophilus influenzae | No | Normal | 1 | Normal | 1 | 98 | ..... |
| | | | | | | | 30 | Normal | 12 | 120 | 96 |
| 3. | Normal | 0 | 23 months | Hemophilus influenzae | No | Mildly abnormal | 1 | Normal | 1 | 100 | ..... |
| | | | | | | | 8 | Normal | 8 | 96 | Refused |
| | | | | | | | 30 | Refused | .... | ..... | ..... |
| 4. | Normal | 0 | 8 months | Hemophilus influenzae | No | Normal | 1 | Normal | 1 | 100 | ..... |
| | | | | | | | 28 | Normal | 10 | 100 | 92 |
| 5. | Behavior problem and abnormal EEG | 1+ | 16 months | Hemophilus influenzae | No | Normal | 12 | Mildly abnormal | 1 | 106 | 122 |
| | | | | | | | | | 6 | 130 | ..... |
| | | | | | | | 30 | Mildly abnormal | 12 | 100 | ..... |
| 6. | Retarded behavior problem | 2+ | 1 week | Hemolytic streptococcus | No | Normal | 12 | Normal | 1 | 100 | 75 |
| | | | | | | | 30 | Abnormal | 10 | 100 | ..... |
| | | | | | | | .... | ..... | 21 | 82 | ..... |
| 7. | Seizures, behavior problem | 2+ | 14 months | Hemophilus influenzae | No | Abnormal | 12 | Abnormal | 1 | 100 | ..... |
| | | | | | | | 30 | Abnormal | 6 | 100 | 105 |
| | | | | | | | .... | ..... | 12 | 110 | ..... |
| 8. | Seizures, retarded | 3+ | 10 months | Hemophilus influenzae | Yes, with operation | Mildly abnormal | 6 | Abnormal | 1 | 100 | ..... |
| | | | | | | | 12 | Normal | 5 | 73 | 46 |
| | | | | | | | 30 | Abnormal | 7 | 81 | ..... |
| | | | | | | | .... | ..... | 18 | 75 | ..... |
| 9. | Decerebrate | 4+ | 2 months | Pneumococcus | Yes, with operation | Abnormal | 6 | Abnormal | 1 | 30 | ..... |
| | | | | | | | 12 | Abnormal | 10 | 8 | Decerebrate |
| 10. | Decerebrate | 4+ | 5 months | Sterile | Symptoms, but negative tap | Very abnormal | 6 | Abnormal | 1 | 20 | ..... |
| | | | | | | | 12 | Abnormal | 12 | 18 | Decerebrate |

persistently abnormal nonfocal electroencephalograms, slow development); 2+ indicated one "major" manifestation (seizures, retardation, neurological deficit) plus any minor manifestations; 3+ indicated two major manifestations plus any minor manifestations; 4+ indicated a decerebrate state.

In addition, using hospital records, the 69 cases of purulent meningitis occurring in children 16 years of age and under treated at the UCLA Hospital between 1955 and 1961 were analyzed retrospectively for age, organism and mortality.

## Results

The ten cases are rated in Table 1. Four received a score of 0, one received a score of 1+, two of 2+, one 3+, and two 4+. The total incidence of apparent neurological damage, then, was six of ten.

*Age.* All the ten patients were under two years at the onset of disease, and the range was from one week to 23 months. In this small series no relationship could be found between the age at onset of meningitis and the severity of the sequelae.

*Organism Cultured.* There were seven cases of *Hemophilus influenzae,* one of pneumococcus, one of streptococcus, and one sterile (received antibiotics before admittance to hospital). Sequelae from *Hemophilus influenzae* meningitis ranged from 0 to 3+. The pneumococcal and sterile cases were the most severely affected.

*Subdural Effusion.* Three of the ten had positive subdural taps. In one the condition resolved with repeated taps and the patient is apparently normal today. In the other two surgical operation was necessary, and both have severe sequelae. One other patient had symptoms suggestive of effusion but subdural taps were negative. This patient became decerebrate.

*Electroencephalograms.* An abnormal electroencephalogram during or immediately following the acute illness occurred in six of the ten cases and was characterized by nonfocal generalized low-potential slow waves of 3 to 5 per second. In four this abnormality persisted and was associated with later evidence of brain damage, the tracings showing the same general pattern as in the acute phase. Of the four patients with normal electroencephalograms during the acute stage, two later had abnormal electroencephalograms and symptoms of mild brain damage.

*Developmental Testing.* Testing identified the four patients with retardation. One normal result of such testing was not enough, as two of these four patients with normal result following the acute stage subsequently had a drop in developmental quotient which persisted and was later confirmed by intelligence testing.

*Intelligence Testing.* Four of the nine tested had significant retardation. One family refused this testing.

Data comparing the severity of sequelae with the source of infection, interval of illness before diagnosis, treatment before diagnosis and severity of acute illness were collected but will not be presented here.

*Population Characteristics.* Interest in the type of population these ten patients came from led to an analysis of the total of 69 cases of childhood purulent meningitis of record at this hospital. Analysis by age and organism is shown in Table 2. The majority of patients was under two years of age, and the predominant organism was *Hemophilus influenzae.* The mortality rate for the total group was 7.3 per cent.

## Discussion

The possibility, suggested in the present study, that subdural effusion has a damaging effect is supported by two other reports. McKay and coworkers[11] found retrospectively that 16 of the 18 patients in their series who had "gross neurological and mental residue" had symptoms suggestive of subdural effusion. Johnson[10] prospectively found a significant fall in intelligence quotient testing in seven of the nine patients in his series who had positive subdural taps. Since the number of cases

TABLE 2.—*Age and Organism in 69 Cases of Purulent Meningitis (1955-1961)*

| Organism | Age of Patient at Onset | | | | | | | Total Number of Patients |
|---|---|---|---|---|---|---|---|---|
| | 0-6 mo. | 6 mo.-1 yr. | 1-3 yr. | 4-6 yr. | 7-9 yr. | 10-12 yr. | 13-15 yr. | |
| Hemophilus influenzae | 3 | 10 | 11 | 5 | 6 | .... | .... | 35 |
| Pneumococcus | 2 | .... | .... | 2 | 2 | .... | .... | 6 |
| Streptococcus | 3 | .... | .... | .... | .... | .... | .... | 3 |
| Pseudomonas | 1 | .... | 1 | .... | 1 | .... | .... | 3 |
| Escherichia coli | 1 | .... | .... | .... | .... | .... | .... | 1 |
| Klebsiella | 1 | .... | .... | .... | .... | .... | 1 | 2 |
| Meningococcus | 1 | .... | .... | .... | .... | .... | .... | 1 |
| Neisseria intercellularis | 1 | .... | .... | .... | .... | .... | .... | 1 |
| Unknown | 6 | .... | 3 | 1 | 3 | 2 | 2 | 17 |
| Total | 19 | 10 | 15 | 8 | 12 | 2 | 3 | 69 |

in all these studies was small, whether or not this relationship is truly causal or just associational remains obscure.

The prognostic value of developmental testing was demonstrated both in the present study and in the only other reported study[6] in which this technique was used. Its value lies mainly in suggesting which patients have a high risk of compromised brain function, and it should not be considered a final judgment.

The population characteristics in Table 2 are similar to those of other reports in the literature with the exception of the low incidence of meningococcal meningitis. The mortality rate of 7.3 per cent among the 69 patients in the present study is compared with the mortality reported in the literature (Table 3). In recent years there has not been a significant further decrease in mortality. A closer look at the deaths in this study may shed some light on this item. In four of the five fatal cases the patient had "secondary" meningitis (a primary disease of the central nervous system afforded obvious direct portal of entry for organisms) as it followed operation for brain tumor in two and complicated a myelomeningocele in two. If all the cases of "secondary" meningitis which occurred in the series are removed, then there is one death in 61 cases, or 1.6 per cent.

The incidence of permanent sequelae in this study is compared with previous reports in Table 4. The data are too diverse to draw any direct comparisons, but there is not a dramatic decline in these figures with the advent of chemotherapy such as was seen in the mortality table.

It appears, then, that the wastage of this disease, while changing in character, may remain significant and needs further investigation.

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TABLE 3.—*Mortality Rate in Childhood Purulent Meningitis (From Literature)*

| *Reported by* | *Date* | *Mortality Rate (Per cent)* |
|---|---|---|
| Worster-Drought[17] | 1918 | 50 |
| Slesinger[15] | 1933 | 32 |
| Crook, et al.[2] | 1941–48 | 21 |
| Smith[16] | 1944–54 | 31 |
| Platou, et al.[13] | 1951–55 | 15 |
| Desmit[6] | 1955 | 9 |
| Carson, et al.[1] | 1956 | 10 |
| Johnson[10] | 1960 | 9 |
| Present study | 1955–61 | 7 |

TABLE 4.—*Sequelae in Childhood Purulent Meningitis*

| *Reported by* | *Date* | *Incidence of Over all Sequelae (Per cent)* | *Comment* |
|---|---|---|---|
| Batten (Cited by Worster-Drought[17] | 1915 | 35 | Infants only |
| Worster-Drought[17] | 1918 | 8.3 | Survivors only |
| Slesinger[15] | 1933 | 36 | |
| Degan[5] | 1940 | 15 | Survivors only |
| Davies[4] | 1940–47 | 67 | Survivors under 2 years |
| Crook, et al.[2] | 1941–48 | 24 | Survivors under 2 years |
| Smith[16] | 1944–54 | 18 | Retrospective |
| Scholz[14] | 1946–51 | 33 | Pneumococcal only |
| McKay[11] | 1945–48 | 24 | Hemophilus influenzae only |
| Daisley[3] | 1950 | 21 | Pneumococcal only |
| Platou, et al.[13] | 1951–55 | 23 | Survivors under 6 years |
| Desmit[6] | 1955 | 14 | |
| Dzherdzheryan[7] | 1959 | 9 | Meningococcal only |
| Haggerty[9] | 1935–60 | 75 | Neonates only |
| Present Study | 1955–61 | 60 | Under 2 years |

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